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Self-Mutilation and Pharmacotherapy

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ABSTRACT: ***Objective:*** **To critically review clinical reports on the pharmacotherapy of self-mutilation.** ***Methods:*** **PubMed search and review of articles dating back to 1950 contributing to the understanding of self-mutilation and its treatment, with a special focus on pharmacotherapy. Key word searches include self-mutilation, deliberate self-harm, and pharmacotherapy of borderline personality disorder.** ***Results:*** **Clinical reports specifically demonstrating reductions in self-mutilation mainly consist of open studies and case reports. These reports support the use of SSRIs, naltrexone, atypical antipsychotics, mood stabilizers, and clonidine in the treatment of self-mutilation. Better constructed studies demonstrate general reductions in impulsive aggression, often in the context of borderline personality disorder, through treatment with antidepressants, antipsychotics, and mood stabilizers.** ***Conclusion:*** **There is evidence, albeit limited, for the pharmacologic management of self-mutilation. Further studies, especially double-blind, placebo-controlled trials, are needed to substantiate these preliminary findings.**

Pathologic self-mutilation is difficult to adequately define, understand, and treat. However, it is not uncommonly encountered in clinical practice. In general, self-mutilation may be defined as any self-directed, repetitive behavior that causes physical injury.[1] It may also be defined as, "the deliberate alteration or destruction of body tissue without conscious suicidal intent."[2]

With the above definitions as a starting point, self-mutilation is further divided into four categories: Severe, stereotyped, socially accepted, and superficial or moderate self-mutilation.[3] Severe self-mutilation is extensive body damage often performed in psychotic or illicit drug-induced states. Stereotyped self-mutilation has a repetitive rhythm, and is often seen in mental retardation and developmental disorders. Socially accepted self-mutilation includes tattooing, ear piercing, and culturally based behaviors. This review article focuses on superficial or moderate self-mutilation, which, as the name implies, often involves multiple forms of self-injury that cause tissue damage of low severity and without lethal intent. Armando Favazza[4] further divided superficial/moderate self-mutilation into three subtypes: Compulsive, episodic, and repetitive. The episodic and repetitive subtypes are considered impulsive in nature and often involve skin burning and/or cutting. The difference between episodic and repetitive self-mutilation is often a matter of degree, with episodic self-mutilation an occasional reflex response to stress or life events that may transition into more repetitive self-mutilation

involving ruminating on the act and/or self-identification as a self-mutilator. With both episodic and repetitive self-mutilation, there is usually little resistance to the urge, with the self-mutilation often experienced as gratifying on some level and ego-syntonic.

In contrast, compulsive self-mutilation is often habitual and more closely related to obsessive-compulsive disorder than disorders with prominent impulsivity, like borderline personality. The self-mutilation may be part of a ritual involving obsessional thoughts. The urge may receive greater resistance and be experienced as ego-dystonic. Compulsive self-mutilation often involves severe nail biting, trichotillomania, or skin picking.[4,5]

Self-mutilation has been assessed through a number of tools that have both clinical and research applications. Scales that have been found to have both validity and reliability tend to involve self-report. It is felt that subjects may be more comfortable endorsing self-mutilation in this format, as opposed to giving a verbal report. The Self-Harm Behavior Questionnaire (SHBQ) differentiates among variable levels of suicidality, assessing self-harm history, frequency, risk, disclosure, and treatment.[6] The Functional Assessment of Self-Mutilation (FASM) is a measure of the methods, functions, and frequency of these behaviors. Participants are asked how often they engaged in 11 different methods of self-mutilation in the previous 12 months, age of onset, and how often they engaged in self-mutilation for each of 22 different reasons.[7] The Self-Harm Inventory (SHI) is another self-report measure of intentional self-harm, including self-mutilation, and has been found to be predictive of borderline personality disorder.[8]

Therapeutic approaches to self-mutilation have perhaps been better studied and have stronger evidence for their efficacy than pharmacologic approaches. Suyemoto and MacDonald's[9] survey of mental health professionals confirms that therapeutic approaches involving cognitive restructuring, behavioral modifications, assertiveness training, and teaching alternative coping mechanisms are the common practice. Dialectical behavior therapy (DBT), a variation of cognitive behavioral therapy, has the most empirical support from at least seven well-controlled trials as a psychosocial intervention for borderline personality disorder. These trials demonstrate decreases or trends in terms of decreased intentional self-injury, impulsiveness, anger, and self-mutilation.[10] A psychodynamic, long-term, partial hospital program also decreases self-mutilation in a controlled study.[10]

The focus of this review article is specifically on the pharmacotherapy for the impulsive subset of superficial/moderate self-injurious behavior (SIB).

IMPULSIVE, SUPERFICIAL/ MODERATE SELF-MUTILATION

Impulsive, superficial self-mutilation is commonly performed by nonpsychotic, normal intelligence patients. Skin cutting is the most common form of self-mutilation, followed by skin burning and self-hitting.[11] Superficial self-mutilation commonly involves comorbid conditions, particularly personality disorders. Pattison and Kahan[12] describe a prototype of self-mutilator as including onset in late adolescence, multiple episodes of self-harm, low lethality, multiple forms of self-harm, chronicity, associated depression (and psychosis), five predominant psychological symptoms (despair, anger, aggression, anxiety, and cognitive constriction), and predisposing factors of lack of social support, homosexuality (men), drug and alcohol abuse, and suicidal ideation (women). Even though DSM-IV TR does not have a specific Axis I or II diagnosis for repetitive self-harm of this nature, it is often subsumed under the diagnosis of Impulse Control Disorder NOS or included as one of the criterion for Borderline Personality Disorder (BPD)—recurrent self-mutilating behavior.[13]

EPIDEMIOLOGY AND RISK

The onset of this behavior is most often in adolescence and tends to follow an episodic, recurrent pattern.[14] Approximately 1.5 to 2 percent of adolescents are affected,[15] with up to almost three-percent prevalence found in some studies.[1,16] Nock and Prinstein[17] recently noted rates, derived from prior studies, of self-mutilative behaviors as high as 14 to 39 percent in adolescent community samples and 40 to 61 percent in adolescent psychiatric inpatient samples, with rates decreasing to four percent in the general adult population and 21 percent in adult clinical populations. Other epidemiologic factors include female gender and college age.[3] An examination of self-mutilation is particularly topical given reports that the incidence may be increasing.[18]

Risk factors include substance abuse and/or personality disorders and a history of self-mutilation.[3] Guertin, et al.,[19] also describe conduct problems, anxiety, depression, and eating disorders as occurring with self-mutilation or as precursors to self-harm.[19] A childhood history of family violence, family alcohol abuse, and sexual and phys-

Risk Factors for Self-Mutilation

- Adolescence to college age
- Female gender
- Substance abuse
- Personality disorders
- History of self-mutilation
- Conduct problems
- Anxiety
- Depression
- Eating disorders
- Childhood history of family violence, family alcohol abuse, or sexual and physical abuse

ical abuse is also linked to self-mutilation in adolescence.

Self-mutilation is also an important risk factor itself in terms of psychiatric morbidity and mortality. Patients with BPD and self-mutilation have twice the risk of suicide compared to patients with BPD without SIB.[20] Cooper, et al.,[31] point out self-mutilation as an independent predictor of subsequent suicide up to four years after a self-mutilation episode. Zlotnick, et al.,[22] also find that the number of different types of self-mutilative behaviors in the past year has a strong relationship to later suicide attempts.

PSYCHODYNAMIC/ INTERPERSONAL FACTORS

There are a number of ways to understand why someone would engage in such disturbing behaviors. It is generally acknowledged by patients and clinicians alike that self-mutilation may be a way, albeit maladaptive, to express or terminate emotional turmoil.

Gunderson's[23] functional models serve as tools to explain how self-mutilation may be attempts at coping. There is an environmental model (psychologically, injury is connected with care), a drive model (antisuicide, self-mutilation as a compromise between life and death drives, and sexual functions, gratification, or punishment), a model of affect regulation (control over intense emotions or device to end or mark dissociative episodes), and a boundaries model (delineating one's own separate, personal existence). For each individual self-mutilator the behavior may actually serve a number of functions seen in the different models.[1,23]

Gunderson's functional models have been supported by the findings of a number of other clinicians and researchers. Individuals who engage in self-harm often have a poor tolerance of anxiety and anger, and the cutting may serve as a temporary way to relieve this dysphoria or create analgesia.[24] Rodham, et al.,[25] also report that many self-cutters want to punish themselves, and that the motives behind self-harm are often less manipulative than thought by clinicians.[25] Nixon, et al.,[5] report that almost half of their sample of self-injuring adolescents endorsed using self-mutilation as a means to stop suicidal ideations or attempts, and that self-mutilation may have a role in inducing or ending dissociative symptoms. From a dynamic perspective, "the infliction of pain, and the drawing of blood, is an effort at feeling, being alive, and delineating boundaries. Thus, while pathologic, it is not an attempt to die but to live."[26]

Self-mutilation can also be seen as linked to impulse control on a number of levels. It has a pattern of urges to cut, tension or arousal before cutting, and momentary pleasure and relief of tension after the act, similar to what is seen in obsessive-compulsive disorder or addictions.[3] The addictive qualities of self-mutilation may explain increasing frequency and severity of self-injury over time in order to achieve the same effect as before.[5] Self-mutilation is also often seen in disorders that have a strong component of impulsivity, including borderline personality, antisocial (especially when incarcerated), and eating disorders, especially bulimia.[27]

NEUROBIOLOGICAL CONTRIBUTIONS

Serotonin system. Decreased serotonin levels have been linked specifically to the trait of impulsivity.[3] There is strong evidence linking decreased serotonin levels with

self-mutilation and disorders that often include self-mutilation. Coming full circle, self-mutilation is often impulsive, with almost 50 percent of adolescents thinking about the act less than one hour beforehand.[25]

Opiate system. In addition to the neurotransmitter serotonin and impulsivity, the opiate pathway is also implicated in both the etiology and treatment of self-mutilation.[28] One-half to two-thirds of borderline patients with self-mutilation experience little or no pain associated with these behaviors. It is hypothesized that there may be a habituation to high levels of endogenous opioids in childhood caused by recurrent exposure to physical and/or sexual abuse. When self-mutilators are tested during a distressed state of mind, their pain thresholds are even higher.[29] These patients may need supranormal levels of endorphins to cope with stress as adults. A decrease in pain sensitivity after early traumatic experiences is reported in animals and humans. Another hypothesized mechanism is instability of endogenous opioids with both high and low levels occurring at different times in the same patient and dysphoria associated with temporarily low levels. Yet another theory considers the possibility that self-injury may involve a form of addiction to endogenous opioids.[30] However, some of the most compelling evidence for a mechanism for attenuated pain perception comes from a recent study involving laser-evoked potentials and psychophysical methods with findings that suggest altered intracortical processing similar to meditative states.[31]

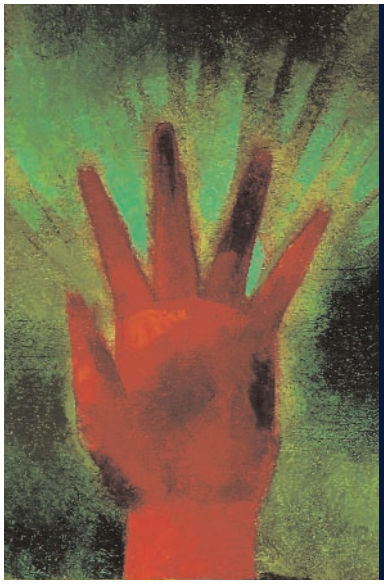
Dopamine system. In addition to serotonin and opioids, dopamine is also implicated in self-mutilation.[27] Self-injurious behaviors are seen in individuals with Lesch-Nyhan syndrome and sometimes Tourette syndrome, which are both disorders that may involve dysregulation of dopaminergic activity and dopamine receptor supersensitivity. Self-biting behavior has also been elicited by administration of stimulants. As will be discussed later, dopamine antagonists may have some degree of success at decreasing self-mutilation.

PHARMACOTHERAPY OF SELF-MUTILATION

Antidepressants. Targeting the hypothesized neurobiological mechanisms of action, several open-label reports look specifically at the response of self-mutilation to pharmacotherapy. An open-label trial of fluoxetine testing the role of serotonergic dysfunction in impulsive self-mutilation in borderline or schizotypal personality disorders reports significant reductions in self-injury.[32] The study is a 12-week prospective trial involving 22 outpatients who were titrated up to 80mg of fluoxetine. Twelve of the patients had a history of recent self-mutilation, specifically cutting. The participants took a short questionnaire quantifying their self-injurious behavior. Fifty-percent fewer individuals were self-injurious (n=6) nine weeks into the study, and the total number of self-mutilative episodes demonstrated a nearly 75-percent reduction. Only two of the initial 12 were still involved in cutting at the end of the 12 weeks, and the episodes occurred less than once a week, a nearly 100-percent reduction. However, no physical examinations were performed to substantiate the findings of the questionnaire. Markovitz also performed an open-label trial of sertraline, average daily dose of 322mg, which dropped the number of self-injurious patients from 11 to 2 and also decreased the number of episodes of self-injury per week after one year of treatment.[33]

There is at least one case report describing remission of self-mutilation, albeit of a compulsive nature, through the use of a SSRI. Fluoxetine successfully treated an 11-year-old boy for compulsive chewing of his fingers with lack of pain sensation.[34]

Opiate antagonists. There are a number of nonblind trials testing the possible role of the endogenous opiate (analgesic) system in self-mutilation through the administration of the opioid antagonist, naltrexone. Sonne, et al.,[35] followed five female patients with borderline personality disorder for a three-week trial that included naltrexone ranging from 50 to 100mg/day given during the second week. Scores from the modified YBOCS demonstrated a significant decrease in self-injurious thoughts when comparing naltrexone treatment with post-treatment. All five patients engaged in self-injurious behavior at baseline, but only one patient self-mutilated while receiving naltrexone. Roth, et al.,[28] also performed an open-label trial of naltrexone with seven female patients with SIB accompanied by analgesia and dysphoria reduction.[28] The mean follow-up period was over 10 weeks, and they were administered 50mg/day of oral naltrexone. Six of the seven patients ceased SIB entirely during the naltrexone treatment, and all patients demonstrated a reduction in their SIB. Four of the seven patients attempted self-mutilation after taking naltrexone, and all reported that analgesia was reversed with lost dysphoria reduction. A double-blind, placebo-controlled study in mentally retarded adults with



DRUG KEY (Trade Names)

alprazolam (Xanax®) • carbamazepine (Tegretol®)
clozapine (Clozaril®) • divalproex sodium (Depakote®)
fluoxetine (Prozac®) • fluvoxamine (Luvox®)
haloperidol (Haldol®) • lamotrigine (Lamictal®)
olanzapine (Zyprexa®) • quetiapine (Seroquel®)
risperidone (Risperdal®) • thiothixene (Navane®)
topiramate (Topamax®) • venlafaxine (Effexor®)

SIB did fail to show any clinical value for treatment with naltrexone,[36] but SIB in patients with normal intelligence may have distinct neurobiological mechanisms and/or behavioral intractability.

There is at least one case report describing the remission of self-injury with an opiate antagonist. A 50-year-old woman with depression stopped scratching, which had lead to chronic neurodermatitis, with a course of naltrexone.[30]

Atypical antipsychotics and mood stabilizers. Studies that both directly address the target symptom of self-mutilation and involve atypical antipsychotics or mood stabilizers consist of case reports. Risperidone led to the remission of self-mutilation in a patient with borderline personality,[37] and clozapine stopped severe self-mutilation in another patient with borderline personality disorder.[38] A case report also describes improved self-mutilation with topiramate.[39]

Alpha-2 agonists. Clonidine decreased the urge to commit self-injurious behavior in an open study involving patients with borderline personality disorder.[40]

PHARMACOTHERAPY OF AGGRESSION AND IMPULSIVITY

Antidepressants. In addition to the few reports that have focused specifically on the pharmacotherapy of self-mutilation, there are many more reports, including some well constructed studies, that target the symptom clusters of impulsivity and/or aggression, especially in borderline personality disorder. As discussed earlier, there may be a strong link between traits of impulsivity and aggression and self-mutilation.[3] At least three double-blind, placebo-controlled studies looked at the effects of SSRIs on impulsivity and/or aggression.[41] Salzman, et al.,[42] found decreases in anger and depression scores when 13 of 22 patients were treated with fluoxetine for 12 weeks. However, these borderline patients did not have any history of self-mutilation. Coccaro, et al.,[43] also found an improvement in impulsive aggression with fluoxetine treatment in a 12-week, double-blind, randomized study in subjects suffering from a variety of impulsive personality disorders. However, while both studies demonstrate statistical significance, the clinical significance is uncertain. In addition, Rinne, et al.,[41] did not find an improvement in impulsivity and aggression when using the SSRI fluvoxamine in a six-week, double-blind, placebo-controlled study with borderline patients. However, the dose of fluvoxamine was only titrated up to a maximum of 150mg/day.

There are also a number of open-label trials of fluoxetine in personality-disordered patients, showing some degree of efficacy in decreasing anger, irritability, and aggression.[44] Markowitz and Wagner[45] also conducted an open-label trial of venlafaxine for BPD with overall Symptom Checklist-90 scores decreasing significantly over time.

Mood stabilizers. There are also similarly constructed controlled studies with the mood stabilizers, divalproex sodium, carbamazepine, lithium, and omega-3-fatty acids. Divalproex was superior to placebo for treatment of patients with Cluster B personality disorders and impulsive aggression in a multicenter, randomized, double-blind study. There was not a trend seen specifically for assault against self, but no subjects with baseline self-injury were included in the study.[46] Carbamazepine demonstrated efficacy in decreasing impulsive

aggression, defined as "behavioral dyscontrol" (including overdoses, self-burning, cutting, violence, and rage episodes) in a double-blind, crossover trial performed by Gardner and Cowdry.[47] A placebo-controlled trial of lithium demonstrates decreased anger and suicidal symptoms in BPD patients.[44] Omega-3-fatty acids lowered impulsive aggression in patients with borderline personality in a controlled study.[48]

Lamotrigine also shows some promise in the treatment of impulsive aggression as demonstrated in an open case series of BPD patients.[49]

Antipsychotics. Antipsychotic agents also have been studied in the treatment of impulsive aggression. Despite some efficacy seen in double-blind, placebo-controlled trials of thiothixene[50] and haloperidol,[51] Hollander, et al.,[44] conclude that, "no double-blind study has demonstrated neuroleptics to be both effective and well tolerated in the treatment of individuals with BPD." However, following Hollander, et al.'s report, there have been two published double-blind, placebo-controlled studies of olanzapine and a presentation of a double-blind, placebo-controlled trial of risperidone in the treatment of borderline personality disorder. Bogenschutz and Nurnberg[52] only found a difference in AIAQ (Anger, Irritability, and Assault Questionnaire) at the eight-week mark of their 12-week olanzapine study, and Zanarini and Frankenburg[53] found improvement over time in all of the symptom areas of the Symptom Checklist-90 during treatment with olanzapine, except for depression. The risperidone trial presented in 1998[52] did not find a significant difference between risperidone and placebo for BPD. However, in an open-label risperidone trial by Rocca, et al.,[54] they find a significant reduction in aggression. A randomized, double-blind study of fluoxetine, olanzapine, and the olanzapine-fluoxetine combination (OFC) without a placebo group finds all three treatments to be safe and effective in ameliorating the impulsive aggression of borderline personality, with olanzapine monotherapy and OFC superior to fluoxetine (mean dose of only 15mg) alone.[55]

Three open-label trials of clozapine also find significant improvement in BPD patients,[52] with Chengappa, et al.,[56] looking specifically at self-mutilation and aggression in BPD (with comorbid psychosis). An open case series of quetiapine demonstrates some efficacy in the treatment of impulsivity, irritability, and aggression in antisocial personality.[57] An open-label study of ziprasidone also demonstrates a lowering of impulsivity in acutely ill borderline personality disorder patients.[58]

PHARMACOTHERAPY OF SELF-MUTILATION: GENERAL GUIDELINES

Based upon review of the available drug studies that target either self-mutilation directly or the impulsive aggression of personality disorders, the following recommendations for pharmacotherapy of self-mutilation can be made. This is in light of the fact that that there is no US Food and Drug Administration (FDA)-approved pharmacological treatment for either self-mutilation or borderline personality disorder. These guidelines share strong similarities with the published recommendations of Soloff[59] for the psychopharmacology of BPD.

SSRIs are proposed as the first-line treatments for dysregulation of impulsive behavior.

Key Points—Pharmacotherapy Guidelines

- SSRIs are proposed as the first-line treatments for dysregulation of impulsive behavior.
- Low-dose atypical antipsychotics are suggested as a second-line treatment, given their efficacy against impulsive behavior.
- Lithium or the anticonvulsant mood stabilizers may be considered for resistant cases.
- Benzodiazepines generally should be avoided, unless other treatment alternatives are poorly tolerated or are of insufficient benefit or the patient has demonstrated prior benefit from benzodiazepines.

Future Directions in Research

- Studies that specifically target the symptom of self-mutilation
- Studies that overcome the limitations of studies in the past (e.g., small sample sizes, female predominance, lack of controls, low dosing, short trial durations)
- Investigation of new generation antidepressants, naltrexone, clonidine, omega-3-fatty acids, atypical antipsychotics, and mood stablilizers
- Investigation of the potential efficacy of polypharmacy
- Investigation of the potential efficacy of combined medication and psychotherapy, especially DBT.

SSRIs generally have a more benign side effect profile than the pharmacologic alternatives. However, destabilization of borderline illness is a potential, though debatable and likely uncommon, adverse effect.[48,60] Weintrob[61] describes self-scratching as a form of self-mutilation that may be secondary to paroxetine.

Low-dose atypical antipsychotics are then suggested as a second-line treatment, given their efficacy against impulsive behavior. Finally, lithium or the anticonvulsant mood stabilizers may be considered. Although not mentioned by Soloff, naltrexone, clonidine, or omega-3-fatty acids can also be considered in cases of self-mutilation refractory to the other treatment regimens.

Benzodiazepines should generally be avoided, unless other treatment alternatives are poorly tolerated or of insufficient benefit or the patient has demonstrated prior benefit from benzodiazepines. Benzodiazepines, specifically alprazolam, potentially increase episodes of "behavioral dyscontrol" (a category that includes impulsive aggression, including, but not limited to self-mutilation) and suicidality.[62]

LIMITATIONS OF PHARMACOTHERAPY

Despite a number of studies addressing pharmacotherapy of self-mutilation and impulsive aggression, the strengths of the studies tend to be outnumbered by their limitations.

Double-blind, placebo-controlled studies are few and far between, with the majority of the trials taking place in an open-label format. There are even fewer studies looking directly at the symptom of self-mutilation. The treatment effects seen, especially in the double-blind studies, have been modest and often demonstrate statistical significance with unclear clinical significance.

The majority of the study subjects are women and Caucasian. There is a need for studies in adolescents, given that study participants are usually adults even though self-mutilation often starts in adolescence. Patients with comorbid conditions, such as depression and substance abuse, are often excluded. The sample patients are often treatment resistant, especially in the open-label trials. The trials also include small numbers of subjects, high dropout rates (demonstrating also how difficult it can be to retain borderline subjects), and short durations (weeks in the context of often chronic behavioral dyscontrol). There also appears to be significant heterogeneity within the borderline personality disorder diagnosis and even greater heterogeneity when it is assumed that many more individuals self-mutilate but do not necessarily meet criteria for BPD. Pharmacological studies in borderline personality are also prone to high placebo response rates.[42]

Making things even more confusing, most of the studies rely solely on patient self-report without substantiation by a clinician assessment scale or visual inspection of the injury to monitor self-mutilation.

Pharmacotherapy trials rarely specify additional treatments, such as psychotherapy, even though they are often underway during the medication interventions.

There are also legal and ethical deterrents regarding the study of self-mutilative behaviors.

The limitations of these studies highlight the importance of treating any comorbid conditions, especially Axis I disorders, first and foremost, and

investigating available nonpharmacologic approaches to treating self-mutilation.

Combination therapy. A combination of psychotherapy and medication may also be a useful approach. Medications may potentially allow patients to better engage in therapy, calming patients and allowing them to reflect before acting.[10] However, adding fluoxetine to DBT did not provide additional benefits in a 12-week, randomized, double-blind, and placebo-controlled trial of patients with borderline personality.[63] This trial is limited, though, by its small sample size, short duration, reliance on self-report measures, and titration up to a maximum of only 40mg of fluoxetine.

FUTURE DIRECTIONS

Studies are greatly needed that specifically target the symptom of self-mutilation and are constructed to overcome the limitations listed above, including small sample sizes, female predominance, lack of controls, low dosing of medications, and short trial durations. Studies should also further investigate new-generation antidepressants, naltrexone, clonidine, omega-3-fatty acids, atypical antipsychotics, and mood stabilizers. The potential efficacy of polypharmacy should also be investigated, along with combined medication and psychotherapy, especially DBT.

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